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EXAMINER
SLOBODYANSKY, ELIZABETH

ART UNIT	PAPER NUMBER
1652	

NOTIFICATION DATE	DELIVERY MODE
11/21/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

Office Action Summary	Application No.	Applicant(s)	
	10/829,331	HATADA ET AL.	
	Examiner	Art Unit	
	Elizabeth Slobodyansky, PhD	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *22 April 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 08/952,741.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/22/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This application is a continuation of application 08/952,741 now US Patent 6,979,731.

Claims 1-9 are pending.

Claim Objections

Claim 6 is objected to because of the following:

The units of molecular weight are missing on line 12 after "molecular weight of 50,000+5000". Also, it appears that since 50,000 are written with a comma, "5000" should be written in the same manner.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-9 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 1, with dependent claims 2-6, is drawn to a DNA encoding an α-amylase having an amino acid sequence of SEQ ID NO:2 with one or more amino acids substituted, added, deleted or inserted and having the specific substrate specificity. Thus, the claim defines the amino acid sequence of α-amylase as different from SEQ ID NO:2 by at least one residue. However, because the number of amino acids encompassed by "more" is not limited, there is no limitation on the structural homology with SEQ ID NO:2 or a DNA encoding thereof. Therefore, claim 1 is equivalent to a claim that is drawn to a DNA encoding α-amylase of an undefined structure. Such variant and a DNA encoding thereof encompass a great number of molecules, both naturally occurring and synthetic, encoding amino acid sequences some of which may not have any structural homology with SEQ ID NO: 2.

Thus, the claims recite an enormous genus of DNAs encoding variant alkaline liquefying α-amylase from any source characterized only by function and pH optimum.

The Court of Appeals for the Federal Circuit has recently held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as be structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." University of California v. Eli Lilly and Co., 1997 U.S. App. LEXIS 18221, at *23, quoting Fiers v. Revel, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original). To fully describe a genus of genetic material, which is a chemical compound, applicants must (1) fully describe at least one species of the claimed genus sufficient to represent said genus whereby a skilled artisan, in view of the prior art, could predict the structure

of other species encompassed by the claimed genus and (2) identify the common characteristics of the claimed molecules, e.g., structure, physical and/or chemical characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these. Later, ENZO BIOCHEM, INC v. GEN-PROBE INCORPORATED (Fed. Cir. 2002) court adhered to Eli Lilly court by holding that the genus of nucleic acid sequences that hybridize under highly stringent conditions are adequately described because "such conditions dictate that all species within a genus will be structurally similar". In contrast, in the instant case, there is no requirement for structural similarity. There is no adequate written description of the claimed genus because it does not distinguish the claimed genus from others, except by specific function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others such as other amylases. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus□. Similarly with the claimed genus of proteins the functional definition of the genus does not provide any structural information commonly possessed by members of the genus which distinguish the protein species within the genus from other proteins such that one can visualize or recognize the identity of the members of the genus.

In the instant specification the genus of genus of DNAs encoding variant alkaline liquefying α-amylase from any source characterized only by function and pH optimum is represented by a single DNA that is a fragment of SEQ ID NO:1 encoding a deletion

mutant of alkaline liquefying α-amylase having the sequence wherein 32 N-terminal amino acids of SEQ ID NO: 2 have been deleted (specification, paragraph bridging pages 11-12).

The specification fails to describe any other representative species by any identifying characteristics or properties other than the functionality of being alkaline liquefying α-amylase with the specific substrate specificity and pH optimum at pH 8-9 and fails to provide any structure: specific function correlation present in all members of the claimed genus nor are they known in the art. Therefore, based on the instant disclosure, it is unpredictable which DNA will encode a mutant alkaline liquefying α-amylase with the desired properties.

Therefore, the specification is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus.

Claim 5 depends from claim 1 and limits the properties of the protein reciting "an isoelectric point higher than 8.5". Claim 6 depends from claim 1 and recites additional physico-chemical properties of an enzyme. Said properties are defined by broad ranges. DNAs encoding said variant amylases encompass a great number of molecules, both naturally occurring and synthetic.

The specification discloses only a single species of the claimed genus, the DNA encoding a N-terminal deletion mutant of SEQ ID NO: 2, *supra*.

The specification fails to describe any other representative species by any identifying characteristics or properties other than the functionality of being alkaline liquefying α-amylase with the specific substrate specificity and pH optimum at pH 8-9

and fails to provide any correlation between the structural and recited physicochemical properties present in all members of the claimed genus nor it is known in the art. Furthermore, the recited physico-chemical properties are the properties of an enzyme not a DNA. Therefore, based on the instant disclosure, it is unpredictable which DNA will encode a mutant alkaline liquefying α-amylase with the desired properties.

Therefore, the specification is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Claims 7-9 are independent claims that are drawn to a DNA encoding alkaline liquefying α-amylase with pH optimum at pH 8-9 from any source comprising a DNA of 20-26 bp not all of which are defined. There is no recitation of any other properties of an enzyme. The DNA of the instant invention (SEQ ID NO:1) is 1776 bp long. Therefore, at most claims 7-9 recite 1.0-1.5% homology with SEQ ID NO:1. The recited structural feature of the genus (i.e., comprise a fragment of 20-26 nucleotides of SEQ ID NO:1) does not constitute a substantial portion of the genus as the remainder of the structure of a polypeptide with the requisite alkaline liquefying α-amylase activity is completely undefined. Fragments consisting of 20-26 nucleotides of SEQ ID NO:1 are highly unlikely to encode α-amylase activity and the specification does not define the remaining structural features necessary for members of the genus to be selected.

Thus, the claims recite an enormous genus of DNAs encoding alkaline liquefying α-amylase from any natural source which would include fungi, plants, animals, etc. as well man made amylases characterized only by function and pH optimum.

The specification discloses only two highly homologous species of the claimed genus, the DNAs encoding alkaline liquefying α-amylase of SEQ ID NO: 2 from *Bacillus* sp. KSM-AP1378 (SEQ ID NO:1) and its N-terminal deletion mutant, *supra*.

The specification fails to describe any other representative species by any identifying characteristics or properties other than the functionality of being alkaline liquefying α-amylase with the specific substrate specificity and pH optimum at pH 8-9 and fails to provide any structure: specific function correlation present in all members of the claimed genus nor they are known in the art. Therefore, based on the instant disclosure, it is unpredictable which DNA will encode an alkaline liquefying α-amylase with the desired properties.

One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. Similarly with the claimed genus of proteins the functional definition of the genus does not provide any structural information commonly possessed by members of the genus which distinguish the amylases species within the genus from other amylases such that one can visualize or recognize the identity of the members of the genus.

Therefore, the specification is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus.

Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Claims 1-9 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a DNA encoding an alkaline liquefying α-amylase having the amino acid sequence of SEQ ID NO:2 and its N-terminal deletion mutant that has a pH-optimum at pH 8-9 and the specific substrate specificity, does not reasonably provide enablement for a DNA encoding an alkaline liquefying α-amylase having an amino acid sequence of SEQ ID NO:2 with one or more amino acids substituted, added, deleted or inserted and having the requisite properties or for a DNA encoding an α-amylase that has a pH-optimum at pH 8-9 and comprising a nucleotide fragment of about 20 bp. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

The claims are broader than the enablement provided by the disclosure with regard to the huge number of all possible nucleic acid sequences encoding alkaline liquefying α-amylase having the specific desired characteristics.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). They include (1) the quantity of experimentation necessary; (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in

the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The nature and breadth of the invention of claims 1-6 encompass any nucleic acid sequence encoding any mutant alkaline liquefying α-amylase having an amino acid sequence of SEQ ID NO:2 with one or more amino acids substituted, added, deleted or inserted and having the specific characteristics from any biological source, or derived by any type of mutation from SEQ ID NO: 2. This reads on any structure without any structural limitations having an alkaline liquefying α-amylase activity with the requisite properties.

The nature and breadth of the invention of claims 7-9 encompass any nucleic acid sequence comprising a partial sequence of 20-26 nucleotides of SEQ ID NO:1 and encoding any naturally-occurring or mutant alkaline liquefying α-amylase having pH optimum at pH 8-9. The specific sequences recited in claims 7-9 represent less than 2% of the entire requisite DNA structure. Thus, with regard to the deficiency of structural limitations claims 7-9 are similar to claim 1. Therefore, one of skill in the art would have been required to make a structure that would impart the requisite properties (claims 1-6) or a structure that comprises a specific 20-26 nucleotide fragment and encodes an α-amylase with pH-optimum at pH 8-9 (claims 7-9).

The specification provides guidance and examples for obtaining DNAs encoding an alkaline liquefying α-amylase having an amino acid sequence of SEQ ID NO:2 from *Bacillus* sp. KSM-AP1378 and its N-terminal deletion mutant. While molecular biological techniques and genetic manipulation to make and use the claimed nucleic acid

sequences are known in the prior art and the skill of the artisan are well developed, knowledge regarding the amino acid residues which are important to the enzymatic activity and folding of the α-amylase, the amino acid residues which can be inserted into or deleted from the amino acid sequence of SEQ ID NO: 2 without affecting the requisite specific enzymatic activity, amino acid homology among α-amylase with said specific enzymatic activity from various biological sources, and the nucleic acid sequence homology among nucleic acid sequences encoding said α-amylase from various biological sources is lacking.

The prior art teaches the DNAs encoding alkaline liquefying α-amylase from *Bacillus* sp. #707 and *Bacillus licheniformis*, respectively (Tsukamoto et al. and Yuuki et al., respectively, form PTO-1449 filed 4/22/04). The DNAs disclosed by Tsukamoto et al. and Yuuki et al. encode the amino acid sequences which have about 87% and 69% identity to SEQ ID NO:2, respectively. However, the disclosed α-amylases have properties different from the α-amylase of the instant invention. In particular, said α-amylases do not have pH optimum at pH 8-9 (see, for example, Response under 37 CFR 1. 116 filed in parent application 08/952,741 on January 14, 2000, pages 7-8). Therefore, the prior art renders it highly unpredictable as to what amino acid residues can be modified in SEQ ID NO:2 without resulting in drastic changes in the properties of the enzyme.

The specification provides no guidance as to what amino acid residues are responsible for the requisite pH optimum and other specific properties imparted by SEQ

ID NO:2 and therefore, what amino acid residues can be mutated without affecting the requisite properties.

Thus, searching for an alkaline liquefying α-amylase or a mutant thereof with desired characteristics is well outside the realm of routine experimentation and predictability in the art of success is extremely low. The amount of experimentation to identify a nucleic acid sequence encoding alkaline liquefying α-amylase with the requisite characteristics of unknown structure is enormous. Since routine experimentation in the art does not include screening vast numbers of genomic or cDNA libraries constructed from large number of biological sources where the expectation of obtaining the desired α-amylase is unpredictable, one skilled in the art would require additional guidance, such as information regarding the biological source of the enzymes and their enzymatic properties and the amino acids which can be mutated without an adverse effect on the function and properties of the enzyme. Without such guidance, the experimentation left to those skilled in the art is undue.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ara et al. (WO 94/26881, form PTO-1449 filed 4/22/04) in view of Yuuki et al. or Tsukamoto et al.

WO 94/26881 is published PCT/JP94/00805. US Patent 5,635,468 is issued on 08/362,493 that is a 371 of PCT/JP94/00805 and is used herein as translation of WO 94/26881.

Ara et al. teach α-amylase from *Bacillus* sp. KSM-AP1378 having the properties identical to the α-amylase from *Bacillus* sp. KSM-AP1378 of the instant invention (US 5,635,468, abstract, Figures 1-4, column 2, lines 54-67; column 4, line 40 - column 5, line 48; claims 1-10). They teach 10 amino acids sequence contained in its N-terminal region (claim 8). Said sequence corresponds to residues 37-46 of SEQ ID NO:2 of the instant invention.

Yuuki et al. and Tsukamoto et al. (form PTO-1449, *supra*) teach a DNA encoding an alkaline liquefying α-amylase from *Bacillus licheniformis* and *Bacillus* sp. #707, respectively. They disclose vectors containing said DNAs.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to isolate a DNA encoding an alkaline liquefying α-amylase from *Bacillus* sp. KSM-AP1378 following the procedures taught by Tsukamoto et al. and Yuuki et al. It would have been further obvious to make deletion mutants of said DNA encoding mature enzyme, for example. Both Yuuki et al. and Tsukamoto teach signal peptides in both amylases. The motivation is provided by Ara et al. who taught the amylase of *Bacillus* sp. KSM-AP1378. One skilled in the art would have a reasonable

expectation of success because the amylases of Yuuki et al. and Tsukamoto et al. and DNAs encoding thereof have been isolated from *Bacillus* species.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-9 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-7 of U.S. Patent No. 6,979,731. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are drawn to or depend from a DNA encoding α-amylase having the amino acid sequence of SEQ ID NO:2 in which one or more amino acids are substituted, deleted or inserted. Claims 1-7 of US 6,979,731 are drawn to or depend from a DNA encoding α-amylase having the amino acid sequence of SEQ ID

NO:2 in which one amino acid is substituted, deleted or inserted. Thus, claims 1-9 encompass claims 1-7 of US 6,979,731. Therefore, claims 1-7 of US 6,979,731 would anticipate or make obvious claims 1-9 of the instant application.

Claims 1 and 3 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-2 of U.S. Patent No. 6,638,748. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are drawn to a DNA encoding α-amylase having the amino acid sequence of SEQ ID NO:2 in which one or more amino acids are deleted and a recombinant DNA encoding thereof. Claims 1-2 of encompass claims 1-7 of US 6,638,748 are drawn to a DNA encoding a fragment of SEQ ID NO:2, i.e. SEQ ID NO:2 in which one or more amino acid are deleted and a recombinant DNA encoding thereof. Therefore, claims 1-2 of US 6,638,748 would anticipate or make obvious claims 1 and 3 of the instant application.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth Slobodyansky, PhD whose telephone number is 571-272-0941. The examiner can normally be reached on M-F 10:00 - 6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, PhD can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

E. Slobodyansky

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Primary Examiner
Art Unit 1652

November 12, 2007